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ABSTRACTS

This section of the JOURNAL *is published in collaboration with the two abstracting Journals,* ABSTRACTS OF WORLD MEDICINE *and* OPHTHALMIC LITERATURE, *published by the British Medical Association. The abstracts are divided into the following sections: Syphilis (Clinical, Therapy, Serology, Pathology, Experimental), Gonorrhoea, Non-Gonococcal Urethritis and Allied Conditions, Chemotherapy, Public Health and Social Aspects, Miscellaneous. After each subsection of abstracts follows a list of articles that have been noted but not abstracted. All subsections will not necessarily be represented in each issue.*

SYPHILIS (Clinical)

Prevention of Congenital Syphilis by Treatment of Syphilis in Pregnancy. NELSON, N. A., and STRUVE, V. R. (1956). *J. Amer. med. Ass.*, **161**, 869. 1 fig.

The authors have studied the incidence of syphilis among 1,279 children from 423 familes in which an infant born late in 1950 or in 1951 was under observation by the Baltimore City Health Department because of a known history of syphilis in the mother. Since 59 of the children were known to have been born before infection of the mother, these were excluded, leaving 1,220 to be studied, 247 of whom were born to untreated mothers. The children of treated mothers were divided into two groups:

(1) those whose mother had received one or more courses of treatment before delivery (799);
(2) those whose mother had received less than one course of treatment (174).

A "course" (which might be intensive or extensive, with arsenic and bismuth or with penicillin, or with a combination of remedies) is defined [somewhat vaguely] as "the amount of treatment that was held to be desirable at the time the mother was treated and given within a reasonable period without excessive treatment delinquency". A child was considered free from congenital syphilis "even though conclusive examination was not made" at the time of the present inquiry if:

(1) no serological or clinical evidence of the disease could be found at 3 months of age;
(2) the mother was serologically negative before delivery and had not relapsed;
(3) the mother had congenital syphilis.

Altogether, 43 congenital infections were discovered among the 1,220 children; of these, 33 occurred in children of untreated mothers, giving an incidence of 13·4 per cent. and ten in children of inadequately treated mothers, an incidence of 5·8 per cent. No infection was discovered among the 794 children of adequately treated mothers. These figures, especially in respect of the first group, are considered by the authors to give a conservative estimate of the incidence of congenital syphilis, as in many cases the date of infection of the mother was not known, while little was known about abortions, still births, or neonatal deaths in these families. Moreover, 48 of the first group of children, 32 of the second, and 145 of the third were not examined, so that negative diagnoses in these cases were not conclusive.

The authors conclude from the results of this study that if a syphilitic woman has had at least one course of treatment and has since suffered no relapse or re-infection, there is little or no risk that her children will have congenital syphilis, whatever the interval between treatment and delivery and whatever the results of serological tests at the time of pregnancy. They therefore consider it unnecessary to re-treat the mother during each subsequent pregnancy. *A. Koby*

Third Generation Syphilis. (Die Lues der dritten Generation.) SZEGO, L. (1956). *Derm. Wschr.*, **133**, 560. 1 fig., bibl.

After a short review of the literature on third generation syphilis the author describes a case seen at the Komitatsspital, Nyiregyhaza, Hungary. Only 68 such families which conformed to the strict criteria laid down by Finger and Fournier have been described. In the author's case a 41-year-old mother and her 6-year-old daughter were found to have congenital neurosyphilis. The child's maternal grandmother was known to have had many miscarriages and only her three youngest children survived, all of whom had congenital syphilis. The husband of the mother (the child's father) was found to be free from syphilitic infection. Some syphilitic stigmata were found in both mother and daughter and it is thought noteworthy that the main lesions in both cases were confined to the central nervous system, suggesting that some constitutional factor influencing the site of the lesions may have been concerned.

G. W. Csonka

Untreated Syphilis in the Male Negro. X. Twenty Years of Clinical Observation of Untreated Syphilitic and presumably Non-syphilitic Groups. OLANSKY, S., SCHUMAN, S. H., PETERS, J. J., SMITH, C. A., and RAMBO, D. S. (1956). *J. chron. Dis.*, **4**, 177. 1 fig., 10 refs.

A further report is presented on the Tuskagee study of untreated syphilis in the male negro, conducted by the U.S. Public Health Service, which is unique in that a comparable control group of non-syphilitic individuals

has also been kept under observation. The present communication summarizes the clinical status, especially with regard to cardiovascular abnormalities, of 139 living, untreated members of the study group and 93 of the control group examined in the twentieth year of observation.

Increasing experience has shown that the radiological criteria generally adopted for the diagnosis of uncomplicated syphilitic aortitis are grossly unsatisfactory. While it is possible by this means to make an *antemortem* diagnosis of aneurysm and aortic insufficiency, the diagnosis of uncomplicated aortitis is not possible. A higher incidence of radiological abnormality was found in the cardiovascular system in the syphilitic than in the non-syphilitic group, and although these abnormalities could not all be categorically ascribed to syphilis, the possibility must be considered that syphilis predisposes to severe or premature degenerative vascular changes. After due allowance had been made for the changes consequent on ageing, it was concluded that electrocardiographic abnormalities, cardiac enlargement, arteriosclerosis, and abnormalities of the blood pressure were significantly more common in the syphilitic group. It is stressed, however, that "this is a study of Negro males, of whom it has been said that the cardiovascular system is peculiarly susceptible to attack by the *Treponema pallidum*". Specific manifestations of late syphilis were found in 23 (14·5 per cent.) out of 159 surviving syphilitic patients examined (including some treated cases). In eleven of these 23 cases (none of which had been adequately treated) the lesion was in the cardiovascular system, consisting in aortic aneurysm or regurgitation or both. *Leslie Watt*

Diagnostic Significance of Fundus Changes in Congenital Syphilis. (Zur Frage des diagnostischen Wertes von Augenhintergrunduntersuchungen bei Lues connata.) BÜTTNER-WOBST, W. (1956). *Klin. Mbl. Augenheilk.*, **128,** 710. 2 figs, 6 refs.

Five of 99 children whose mothers were syphilitic showed retinal changes. Their significance is discussed. *G. L. Cantrell*

Ocular Manifestations in Syphilis of the Central Nervous System. (Les manifestations oculaires de la syphilis nerveuse.) BOUDOURESQUES, J., VIGOUROUX, R., and STAM, C. (1955). *Gaz. méd. France*, **62,** 1217.

A pathogenetic and clinical study is outlined, with the conclusion that treatment must be early and intensive. *S. Vallon*

Case of Syphilitic Perineuritis of the Optic Nerve. (Un cas de périnévrite syphilitique du nerf optique.) FAVRE, M. (1956). *Ophthalmologica (Basel)*, **131,** 290. 5 refs.

A case of bilateral papilloedema with unaffected vision is described. There is a short account of the pathology and frequency. *A. A. B. Scott*

Syphilitic Cold Haemoglobinuria. WATSON, K. C., and LAURIE, W. (1956). *S. Afr. med. J.*, **30,** 1001. 7 refs.

Aetiology and Pathogenesis of Interstitial Keratitis. [In Turkish.] ÇOLAKBAYRAKTAR, I. (1955). *Ankara üniv. Tip Fak. Göz Klin. Yill.*, **8,** 43. 6 refs.

Report of the latest trends on the subject. *S. Gördüren*

Syphilitic Gumma of the Hypophysis. (Gomme syphilitique de l'hypophyse.) FRANÇOIS, J., and VERRIEST, G. (1955). *Acta neurol. psychiat. belg.*, **55,** 483. 5 figs.

A case of a 37-year-old woman is reported. Visual acuity was decreased and she had bitemporal haemianopia, as well as systemic disorders. The ocular defects became almost normal after anti-syphilitic treatment. *M. H. T. Yuille*

Symptomatic Macroglobulinaemia in Congenital Syphilis (Case Report). (Symptomatische Makroglobulinämie bei Lues connata.) KOCH, F., SCHLAGETTER, K., SCHULTZE, H. E., and SCHWICK, G. (1956). *Z. Kinderheilk.*, **78,** 283. 3 figs, 40 refs.

Correcting the Reported Incidence of Congenital Syphilis in Philadelphia. INGRAHAM, N. R., and BURKE, M. J. (1956). *Amer. J. publ. Hlth*, **46,** 1309. 3 figs, 15 refs.

Syphilis and Tuberculosis. (Syphilis und Tuberkulose.) STREITMANN, B. (1956). *Klin. Med. (Wien)*, **11,** 398. 37 refs.

SYPHILIS (Therapy)

Experiments on the Use of Hyperthermia in the Treatment of Primary and Secondary Syphilis. [In Russian.] KHOKHUTIN, I. I. (1956). *Vestn. Vener. Derm.*, No. 3, 32.

Hyperthermia was employed in the treatment of early primary and secondary syphilis, in combination with penicillin in 44 cases and with arsenic and bismuth in 67 cases, at the Tomsk Medical Institute. The patients had had no previous antisyphilitic treatment. To induce fever, TAB vaccine was injected intravenously, a course of five or six hyperthermic reactions, each lasting 5 to 10 hrs and repeated every 3 to 5 days, being given. Penicillin was given intramuscularly in a dose of 40,000 units 3 hrly to a total of 5,000,000 units. As a rule, the combined treatment accelerated the disappearance of *Treponema pallidum* from eroded lesions and speeded up the regression of primary and secondary syphilides and enlarged lymph nodes. The serological reactions also became negative more rapidly. The results were better when hyperthermia was combined with penicillin than when metallotherapy was used, two patients failing to respond to the former and five to the latter. The maximum follow-up period was 7 yrs, though the number of patients kept under observation was never large and diminished steadily, only six patients in the first group and three in the second being followed up for longer than 5 yrs. Two patients in the first group and ten patients in the second suffered a serological and clinical relapse within 6 months of treatment, and one

patient in the second group developed asymptomatic neurosyphilis 16 months after completing treatment. The incidence of therapeutic failure was 9 per cent. in the first group and 23·8 per cent. in the second.

H. Makowska

Results of Five Years of Penicillin Treatment of Neurosyphilis. (Ergebnisse 5-jähriger Penicillin-Behandlungen bei Neurosyphilitikern.) ORBÁN, T., and LAZAROVITS, L. (1956). *Wien. med. Wschr.*, **106,** 377. 2 figs, 20 refs.

From the University Neurological Clinic, Budapest, the authors report the results of treatment of 254 patients with neurosyphilis during the 5-yr period 1949–54. Of these patients 56 (22 per cent.) had meningo-vascular syphilis, 74 (29 per cent.) asymptomatic neurosyphilis or pupillary abnormalities only, sixty (24 per cent.) dementia paralytica or tabo-paresis, and 64 (25 per cent.) tabes dorsalis. Examination of the cerebrospinal fluid (CSF) was performed yearly up to 1953 and afterwards at 6-monthly intervals.

In 189 cases treatment was with penicillin alone and in 65 with penicillin and fever therapy. During 1949 penicillin was given in courses to a total dose of 3 to 4·8 mega units each, but after that date this was increased to 6 to 9 mega units. [Most of the patients appear to have received more than one course of penicillin.]

The effects of penicillin alone and of penicillin plus fever therapy are compared. Penicillin alone produced the best results in meningo-vascular syphilis, improvement in the CSF findings occurring in 98 per cent. of these cases and clinical improvement in 22·5 per cent. Of the patients with tabes dorsalis, 5·5 per cent. showed clinical deterioration after treatment with penicillin despite marked improvement in the CSF. In the patients with dementia paralytica and tabo-paresis the results of combined therapy with penicillin and fever were better than with penicillin alone. Relapses, as indicated by the CSF findings, occurred in 16 per cent. of the patients treated with penicillin alone and in only 2 per cent. of those treated with penicillin plus fever. Although among the tabetics, combined penicillin and fever therapy produced a more rapid improvement in the CSF picture, progression of the disease occurred twice as frequently in this group as in tabetic patients treated with penicillin alone. Patients with lightning pains did better on penicillin alone, fever therapy seeming to precipitate attacks of these pains. Of the patients with ataxia 64 per cent. improved on treatment with penicillin alone, whereas combined therapy had a tendency to cause deterioration. There were eight patients with optic atrophy and these were treated with penicillin alone, five showing objective and subjective improvement, but in three the condition remained stationary throughout the period of observation.

In conclusion the authors suggest the following doses of penicillin for the treatment of neurosyphilis: in late asymptomatic and meningo-vascular neurosyphilis 6 to 12 mega units, and in dementia paralytica and tabes dorsalis 12 to 20 mega units. Fever therapy is recommended in cases where penicillin does not produce clinical improvement or in which the CSF does not return to normal after a reasonable period. Fever therapy is further recommended in cases of dementia paralytica, tabo-paresis, and progressive optic atrophy.

R. D. Catterall

Problem of Interstitial Keratitis and Choroido-Retinitis in Congenital Syphilis in Relation to Modern Therapeutics. (El problema de la queratitis intersticial y de la coriorretinitis de la sífilis congénita en relación con las modernas terapéuticas.) MAZZINI, M. A., JONQUIÈRES, E. D. L., and POPPI, M. (1955). *Rev. argent. Dermato-sif.*, **39,** 44. 13 refs.

This includes two case reports of congenital syphilis with ocular manifestations. Both cases (one had bilateral interstitial keratitis, and the other severe choroido-retinitis) were treated with penicillin in high quantities, cortisone, and ACTH. Their bad prognosis was confirmed despite this treatment. *B. A. Weil*

Topical Use of Cortisone in Syphilitic Interstitial Congenital Keratitis. (Aplicación tópica de la cortisona en queratitis intersticial congénita sifilítica. Reportaje de diez casos.) SÁNCHEZ-BEAUJON, R. (1955). *Rev. oftal. venez.*, **1,** 41.

The author reports ten cases treated locally with cortisone acetate (2·5 per cent.) combined with penicillin and local atropine. Cure resulted in eight cases. The author considers this method of treatment harmless, cheap, and applicable in out-patient clinics. *D. Lukić*

Results of Treatment of 188 Cases of Early Syphilis with Penicillin and Bismuth after Five Years. (Resultados obtenidos en el tratamiento de 188 casos de sifilis reciente con penicilina y bismuto al cabo de cinco años.) PARDO, O. A. (1956). *Bol. Soc. cubana Derm. Sif.*, **13,** 35. 5 refs.

Neurosyphilis treated with Achromycin in a Penicillin-sensitive Patient. (Achromycinbehandlet neurolues hos penicillin-overømfintlig pasient.) VOLL, A. (1956). *T. norske Laegeforen.*, **76,** 474.

Certain Aspects of the Treatment of Neurosyphilis. (Ausgewählte Kapitel aus dem Gebiete der Therapie der Neurolues.) ACKERMANN, R. (1956). *Fortschr. Neurol.*, **24,** 470. Bibl.

Combined Treatment of Neurosyphilis with Pyretotherapy, Subdural Iodine, and Bismuth. (Terapia della neurolue: trattamento associato pireto-jodosubdurale-bismutico.) FASANARO, G., and SCOPPA, A. (1956). *Acta neurol. (Napoli)*, **11,** 721. Bibl.

Present Status of the Diagnosis and Treatment of Syphilis. VANDOW, J. E., and SOBEL, N. (1956). *N. Y. St. J. Med.*, **56,** 2796. 18 refs.

SYPHILIS (Serology)

Value of the Nelson Test in the Diagnosis of Congenital Syphilis in Early Infancy. (L'intérêt du test de Nelson pour le diagnostic de la syphilis congénitale dans la première enfance.) ROMAGNY, G. (1956). *Pédiatrie*, **11**, 419.

The author throws some doubt on the absolute reliability of the treponemal immobilization (TPI) test of Nelson in the diagnosis of congenital syphilis, and quotes 29 case histories, some of which seem to suggest that the TPI test may occasionally give false results. Clinicians are familiar with the difficulties in children in the interpretation of routine standard tests for syphilis (STS), in which the greatest difficulty is experienced in the interpretation of "doubtful" reactions. The author regards the TPI test as another laboratory test, more sensitive than the STS, but with definite limitations, its greatest value being as an instrument of research into the transmission of congenital syphilis.

He suggests that treatment, while otherwise successful, may have allowed the persistence of scarcely recognizable forms of abortive congenital syphilis. In doubtful cases, and in cases in which there are inexplicable variations in titre, interpretation may be possible only by long observation and repetition of the tests. The duration of persistence of antibody transmitted to the child is not known, nor is the significance of positive reactions persisting after treatment, although it has been customary to accept a limit of 3 months for a positive STS reaction due to transmitted antibodies. In this field the TPI test has not replaced the earlier routine tests.

Robert Lees

Serological Examinations of Electrophoretically-Separated Serum Components with Cardiolipin Antigen and an "Incomplete" Cardiolipin Antigen (Cardchol). [In English.] SCHMIDT, H., and BIRCH-ANDERSEN, A. (1956). *Acta path. micro-biol. scand.*, **39**, 47. 22 refs.

In order to ascertain in which protein fraction of the blood syphilitic reagins occur, and to investigate the cause of the differences in the reactivity of sera to complete and incomplete cardiolipin antigens, electrophoretic fractionation of ten sera which were thought to have given non-specific reactions with serological tests for syphilis and of two sera from patients with early syphilis was carried out at the State Serum Institute, Copenhagen. Quantitative tests were then carried out on the individual fractions by the Mørch Wassermann technique with both cardiolipin antigen and "cardchol", an incomplete antigen composed of cardiolipin and cholesterol only. Previous work had shown that most syphilitic sera were more reactive with cardiolipin antigen, but that sera giving non-specific reactions often gave higher titres with cardchol than with the complete cardiolipin antigen.

Serological reactivity was demonstrated in both γ- and β-globulin components. It was found that some sera failed to react with cardiolipin before fractionation, although the γ- and β-globulin components were reactive. It is suggested that a factor was present in the albumin+α_1-globulin fraction which inhibited the reaction with cardiolipin but did not affect that with the incomplete antigen, thus offering an explanation of the lower specificity of cardchol. The greater sensitivity of cardiolipin with syphilitic sera may be due to the presence of more than one antilipoidal antibody.

It was not possible to show any correlation between the protein content of the fractions and their serological reactivity or to determine an electrophoretic pattern which indicated a positive reaction with lipoidal antigen.

A. E. Wilkinson

Indication for and Limitations of the Treponemal Immobilization Test (Nelson Test). (Indications et limites du test d'immobilisation des tréponèmes pâles (test de Nelson.) DELACRÉTAZ, J. (1956). *Schweiz. med. Wschr.*, **86**, 645. 27 refs.

From his experience with the treponemal immobilization (TPI) test at the University Skin Clinic, Lausanne, the author suggests two major indications for its performance:

(1) in patients who give a positive reaction to one of the standard serological tests but show no evidence of syphilis;
(2) in patients who are suspected of having late syphilis but in whom standard serological reactions are negative.

He found that the TPI test was highly specific for syphilis and the treponematoses, and considers that a negative TPI test result in patients with treated syphilis may be evidence of cure, although a persistent positive test result is not in itself an indication for further treatment. The exact significance of the latter finding remains as yet uncertain.

G. W. Csonka

TPI Test as a Daily Routine Laboratory Procedure. HARRIS, A. (1956). *Amer. J. publ. Hlth*, **46**, 723. 12 refs.

The results obtained during a 9-month period with the treponemal immobilization (TPI) test which, with certain modifications, is in daily use at the Venereal Disease Research Laboratory, Chamblee, Georgia, are evaluated. Of 1,851 specimens of serum submitted to the laboratory for examination, 126 were unfit for testing; of the remainder, 742 (43 per cent.) gave a positive reaction, 26 (1·5 per cent.) a weakly positive reaction, 940 (54·5 per cent.) a negative reaction, and only seventeen (1 per cent.) gave an inconclusive result. Detailed information regarding the clinical diagnosis was available in respect of 1,700 sera; of these, 205 were from patients believed to have syphilis, 1,267 were thought to have given a false positive reaction, and no opinion was stated in respect of 228. Thus approximately 75 per cent. of the patients were considered to be false positive reactors, and of these 1,267 specimens of serum, 506 gave a positive reaction to the test. Of 98 specimens from patients with a previous history of syphilis, 26 were negative by the TPI test. Of the 205 cases of suspected syphilis a history of syphilis was obtained in 96, and in 75 of these the result of the TPI test was positive; of the 109 cases with no such history, only 64 gave a positive reaction.

It is concluded that in all three categories studied the serum of patients with a history of past syphilitic infection produced a greater percentage of positive findings by the TPI test (75 per cent.) than did those without such a previous history (42·5 per cent.). Approximately one-third (32·2 per cent.) of the sera from patients regarded as having syphilis failed to react to the TPI test. In the biological false positive category a 60 per cent. agreement with the TPI test results was obtained. The over-all agreement between the clinical diagnosis and the TPI test result was approximately 60 per cent.

R. R. Willcox

Detection of Syphilitic Reagin by Means of the Conglutination Reaction. (Recherche de la réagine syphilitique a l'aide de la réaction de conglutination.) FAURE, M., and DAOULAS-LE-BOURDELLÈS. (1956). *Ann. Inst. Pasteur*, **90,** 763. 7 refs.

In this communication from the Institut Pasteur, Paris, the technique of the conglutination reaction is fully described [and should be read in the original, as it does not lend itself to abstracting]. In a comparative study the techniques of Kline and Kolmer and the conglutination reaction were used to detect syphilitic reagin in 87 syphilitic and 274 presumably non-syphilitic sera. Only in three of the 274 controls was the negative reaction in doubt. With the conglutination test the syphilitic sera gave reactions two to eight times as sensitive as those obtained with the Kolmer test; zoning, however, was frequently encountered, and for this reason the reaction should not be used for routine diagnostic purposes, though its high sensitivity may be useful in difficult cases.

G. W. Csonka

Deviating and Flocculating Antilipoidal Reagins in Syphilitic Serum. (Contributo allo studio delle reagine antilipoidei devianti e flocculanti nel siero sifilitico.) PEZZI, R., and BERTANI, C. C. (1956). *Boll. Ist. sieroter. milan.*, **35,** 137. 19 refs.

Stating that there is chemical, serological, and clinical evidence for regarding flocculating and complement-deviating antibodies as distinct types, the authors describe studies carried out at the Istituto Sieroterapico Belfanti, Milan, to elucidate this question and to determine whether the complement-fixing antibody is an incomplete antibody in Race's sense—that is, a blocking antibody producing agglutination in a medium with high protein concentration and giving a positive reaction to the Coombs test.

Flocculation tests with VDRL antigen were carried out on samples of syphilitic serum. After centrifugation a complement-fixation test carried out on the clear supernatant fluid gave a positive result, whereas the same test on the deposit gave a negative one. It is therefore deduced that the complement-fixing antibody does not combine with the flocculating antigen. In a second series of experiments the floccules were washed with sulphuric ether to remove all lipids and cholesterol. The washed floccules then again gave a positive (but weaker) reaction to the flocculation test and also to the complement-fixation test. Thus the flocculating antibody is able to deviate complement.

Flocculation tests were also carried out on sera to which an equal quantity of a 30 per cent. solution of albumin had been added. Neither the floccules filtered off nor the supernatant in this series gave a positive reaction to the complement-fixation test. Thus, it appeared that the complement-deviating antibody flocculated in the high-protein medium like an incomplete antibody. Finally, when serum which gave a positive complement-fixation reaction only and a negative result in the flocculation test was added to flocculation-positive sera it prevented flocculation in these sera. Performance of the Coombs test on these blocking sera gave a negative result—possibly, however, owing to the sequence in which the tests were carried out.

It is concluded that complement-fixing and flocculating antibodies represent two distinct types of antibody. The authors recommend that until the clinical inferences to be drawn from these facts are understood, both the complement-fixation and flocculation tests should be applied.

F. Hillman

Clinical Significance of Hyperglobulinemia. I. Diagnostic Implications. II. Correlation with Liver Function Tests, Serologic Tests for Syphilis, and Bone Marrow Examinations. FEINSTEIN, A. R., and PETERSDORF, R. G. (1956). *Ann. intern. Med.*, **44,** 899, 925. 2 figs. bibl.

In the first part of this study, the object of which was to determine the significance of the isolated laboratory finding of a raised serum globulin level, the authors, working at Yale University School of Medicine, analysed the hospital records of 394 patients in whom a serum globulin level of 3·9 g. per 100 ml. or higher had been noted. Of these patients 268 had diseases generally associated with an elevated serum globulin content, namely, multiple myeloma, sarcoidosis, collagen diseases, liver disease, cancer, chronic pulmonary disease, and certain infections. The remaining 126 were suffering from a variety of disorders not commonly associated with an increase in the serum globulin fraction, such as cardiovascular disease, renal disease, endocrine disorders, and musculo-skeletal diseases.

Of the patients in whom the serum globulin level exceeded 5 g. per 100 ml., over 90 per cent. had specific "hyper-globulinaemic" diseases, about half of them suffering from multiple myeloma, sarcoidosis, or collagen disease. Of those in whom the serum globulin level was between 4·2 and 5 g. per 100 ml., the majority had hepatic disease, metastatic carcinoma, or chronic diffuse pulmonary disease, only a few having multiple myeloma, sarcoidosis, or collagen disease. Lastly, those in whom there was a minimal rise in the serum globulin level (3·9 to 4·2 g. per 100 ml.) had a great variety of unclassified chronic diseases of one or more systems. These findings appear to indicate that a slight elevation of the serum globulin level is of very limited diagnostic significance, whereas a marked elevation frequently indicates a specific pathological process. The authors point out that only 20 per cent. of the patients with hyperglobulinaemia also had hyperproteinaemia, indicating that in the

majority the pathological condition was associated with a fall in serum albumin level, exceptions being sarcoidosis and collagen disease, in which the serum albumin level was approximately normal despite the marked rise in the serum globulin level.

In the second part of this study the authors investigated the relationship between the serum globulin levels and the results of liver function tests, serological tests for syphilis, and bone-marrow examinations carried out on the same series of patients. Abnormalities in the liver function test results in 160 patients without overt hepatic disease were interesting in that they showed a positive correlation with the disturbances in the serum protein pattern. The cephalin-cholesterol flocculation reaction was more likely to be abnormal in the presence of a low serum albumin level, whereas the thymol reaction appeared more sensitive to elevation of the serum globulin level. In this group the thymol test gave a normal result more frequently than did the cephalin test, although both tests gave about the same number of abnormal results in patients with liver disease. Abnormal reactions to the cephalin and thymol tests were found more often in those diseases in which the raised serum globulin level was due mainly to an increase in the gamma-globulin fraction than in those in which there was an increase in all three globulin fractions or mainly in the alpha and beta fractions. The results of the alkaline-phosphatase and "bromsulphalein" retention tests showed no correlation with abnormal serum albumin or globulin values. However, there was abnormal retention of bromsulphalein in many of the patients without liver disease.

False positive reactions to serological tests for syphilis were observed in 4 per cent. of patients, and were unrelated to the diagnosis of the condition or the serum globulin level. "Benign" plasmacytosis was found in fifteen and a diagnosis of multiple myeloma established or confirmed in twelve of the 71 patients in whom bone-marrow examination was performed.

The author's findings are compared with those reported in the literature. *Victor M. Rosenoer*

Cardiolipin Antigen. Nephelometric Measurements. 4. [In English.] REYN, A., HARTMANN, J., and SCHMIDT, H. (1956). *Acta path. micro-biol. scand.*, **39**, 57. 4 figs, 12 refs.

When saline suspensions of cardiolipin antigen are allowed to stand they become more sensitive and their turbidity increases owing to aggregation of particles, the progress of which can be followed by nephelometric measurements. This paper from the State Serum Institute, Copenhagen, describes experiments to determine the effect of serum and serum fractions on this process of maturation.

One part of cardiolipin antigen was mixed with 133 parts of saline, the serum fraction studied added immediately, and serial nephelometric measurements made over a 30-min. period. Human or guinea-pig serum at a concentration of 1 in 500 impaired maturation, syphilitic sera giving weaker reactions with the serum-treated antigen than with untreated antigen at the same interval after preparation. Tests on fractions separated from normal human sera by electrophoresis showed that the inhibitory effect of the albumin+α_1-globulin fraction on maturation was the strongest, being greater than that of the parent serum. The γ-globulin and $\gamma+\beta$-globulin fractions had no inhibitory effect.

Bovine albumin had no definite inhibitory effect on maturation, but syphilitic sera gave weaker reactions with antigen treated with it than with the control after 20 minutes' maturation. Bovine γ globulin inhibited maturation only in the highest concentration tested (1 in 50). Cohn's Fraction IV-1, containing 78 per cent. α-globulins, produced complete inhibition of maturation at a concentration of 1 in 500; cardiolipin antigen treated with this serum fraction gave much less sensitive reactions with syphilitic sera than did untreated antigen. The authors consider that inhibition of nephelometric maturation and of serological activity may be connected with the presence of lipoproteins and that the effect is mainly located in the α-globulins, more especially in the α_1 fraction. *A. E. Wilkinson*

Use of a Medium Containing Freeze-Dried Rat Embryo Extract in the Nelson–Mayer Test. (Sulla realizzazione del test di Nelson–Mayer con l'uso del terreno all'estratto embrionario di ratto liofilizzato.) RESTA, V., and ROSSETTI, C. (1956). *Minerva derm. (Torino)*, **31**, 147.

The authors point out that in performing the Nelson–Mayer test it has been necessary up to now continuously to renew the rat-embryo extract used in the medium, and that this provision has been precariously dependent on a supply of rats in advanced pregnancy. The rate of treponemal survival in the medium as currently used has been such that fresh rat embryos were required every 14 days.

At the University Dermatological Clinic, Padua, the authors have carried out Nelson–Mayer tests in parallel using media containing lyophilized and fresh rat-embryo extracts on negative and positive sera with inactivated and non-inactivated complement, and on saline controls. Only the tests using positive sera and active complement gave complete immobilization. The tests were repeated at fortnightly intervals over 10 months with aliquot portions of the original batch of freeze-dried embryo extract. It was found that such an extract maintained its suitability for the test, and even a slight superiority over the standard medium, throughout the whole period. *F. Hillman*

Microflocculation Reaction with Cerebrospinal Fluid in the Diagnosis of Neurosyphilis. (La reazione di microflocculazione per la diagnosi liquorale di infezione luetica del nevrasse.) COGORNO, A. (1956). *Sistema nerv.*, **8**, 167. 1 fig, 25 refs.

Diagnostic Value of the Microflocculation Reaction to Cardiolipin in Neuropsychiatry. (Valore diagnostico della microreazione di flocculazione alla cardiolipina in neuro-psichiatria.) MARTELLI, G. (1956). *Riv. ital. Igiene*, **16**, 263. 14 refs.

Method of Preparation of Cardiolipin. (Méthode de préparation du cardiolipide.) FAURE, M., and MORELEC-COULON, M. J. (1956). *Ann. Inst. Pasteur*, **91,** 537. 4 refs.

Jacobsthal Complement-Fixation Test with Cardiolipin Antigen. [In English.] VALENTINČIĆ, M., LEBEZ, D., and VOZELJ, M. (1956). *Acta med. iugoslav.*, **10,** 50. 2 figs, 7 refs.

Problems of Syphilitic Serology studied with Different Antigens. (Zur Problematik der Lues-Serologie bei Anwendung verschiedener Antigene.) GREGORCZYK, K. (1956). *Arztl. Wschr.*, **11,** 888. 2 figs.

Serological Diagnosis of Syphilis by De Donno's Technique. (Contributo alla diagnosi sierologica della lues con la metodica di De Donno.) FIORE, C., and BUONDONNO, E. (1956). *Ann. Neuro-psichiat. Psicoanal.*, **3,** 429.

Demonstration of Particulate Adhesion of the Rieckenberg Type with the Spirochete of Syphilis. LAMANNA, C., and HOLLANDER, D. H. (1956). *Science*, **123,** 989. 19 refs.

Basis and Specific Significance of the Serological Diagnosis of Syphilis. (Die Grundlagen und die spezifische Bedeutung der serologischen Luesdiagnostik.) HEYMANN, G. (1956). *Dtsch. med. Wschr.*, **81,** 1505. 1 fig, bibl.

Adjusting of the Colloidal Gold Solution for the Serum Gold Test. [In English.] SCHWARZ, P., and STANULOVIĆ, D. (1956). *Acta med. iugoslav.*, **10,** 59. 8 refs.

Influence of P^{32} upon the Antibody Titer of Incurable Latent Syphilis. NAKAJIMA, T., and HAYASHI, O. (1956). *Tohoku J. exp. Med.*, **64,** 17. 2 refs.

Influence of P^{32} upon the Antibody Titer of Late Rabbit Syphilis. MIZUMOTO, R., and HAYASHI, O. (1956). *Tohoku J. exp. Med.*, **64,** 21. 2 refs.

Incidence of Sero-Positive Syphilis among Married Men in Norway. (Hyppigheten av seropositiv syfilis blant gifte norske menn.) ENG, J. (1956). *T. norske Laegeforen.*, **76,** 476. 12 refs.

SYPHILIS (Pathology)

Morphology of *Treponema pallidum*. SEQUEIRA, P. J. L. (1956). *Lancet*, **2,** 749. 4 figs, 7 refs.

The author, working at the Royal Free Hospital, London, has investigated the morphology of *Treponema pallidum*—mainly the Nichols strain and organisms from two cases of active syphilis—and several other treponemes by dark-field microscopy at a magnification of × 1,500.

Of twenty organisms in a suspension of the Nichols strain examined initially, six appeared to have a left- and six a right-hand spiral, and in eight no evidence of direction was obtained. When observed from various angles as they drifted across the field the organisms did not show the characteristics to be expected of a spiral, and further examination suggested that the curves all lay in one plane. All the static appearances observed under the microscope could be stimulated by wire models of flat wave form, whereas they could not be reproduced with a spiral model without gross distortion. The only feature seen which was inconsistent with the flat form was "rotation round the long axis of the organism, associated with an appearance like the thread of a screw passing along its length". However, detailed study showed that this form of motility consisted in a wave of activity starting at one end or in the middle of the treponeme and passing along it, each loop in turn rotating through about 180°.

The treponemes from active cases of primary syphilis had the same characteristics, as did a strain of *T. pertenue*, but a strain of *Borrelia perfringens* was a true right-hand spiral; moreover, it moved rapidly through the suspending medium when rotating around its long axis, whereas *T. pallidum* showed no such translational movement with similar "rotation". Further examination of more than 200 strains of *T. pallidum* have confirmed that this organism is flat, though the plane in which the waves lie may be twisted through an angle up to 180° over its length.

The taxonomic implications of these findings are briefly discussed, it being pointed out that *T. pallidum*, the type species of the *Treponemata*, does not now appear to conform to the description of the genus.

F. Hillman

Comparative Electron-Microscopical Studies of the Morphology of *Treponema pallidum*, *Treponema pertenue*, and Reiter's Spirochaete. (Vergleichende elektronenmikroskopische Untersuchungen zue Morphologie von Treponema pallidum, Treponema pertenue und Reiterspirochäten.) MÖLBERT, E. (1956). *Z. Hyg. InfektKr.*, **142,** 510. 9 figs, 6 refs.

Electron-microscopical studies of *Treponema pallidum* by various workers have consistently shown the presence of a narrow band of fibrils running the length of the organism and probably responsible for its motility. The present author, writing from the University of Würzburg, asserts that in pathogenic strains of *T. pallidum* (Nichols and Truffi) and in *T. pertenue* this band, which is about 700 Å wide, constantly contains six fibrils, whereas in Reiter's spirochaete there may be between five and twelve though six is usual. The fibrils show transverse striations similar in appearance to those of collagen fibres.

He has also studied the mechanism of multiplication, which was the same in all the above strains. The point at which fission is to occur is indicated by the formation of a granule of denser material, wider than the body of the organism and traversed by the fibrillar band. This granule then becomes constricted and divides transversely, about half going to each daughter treponeme, in which it appears, after division, as a terminal granule

which later disappears. Dividing forms are most numerous in 7-day-old cultures or in rabbit chancres from the 7th to 10th days, but may still be found after 21 days. Multiplication by spore production does not appear to occur. *M. Lubran*

SYPHILIS (Experimental)

Immunity in Experimental Syphilis. The Concept of Cellular Refusal. (A propos de l'immunité dans la syphilis expérimentale. La notion de refus cellulaire.) GASTINEL, P., COLLART, P., and VAISMAN, A. (1956). *Ann. Inst. Pasteur*, **90,** 677. 25 refs.

From previous experiments carried out at the Institut Alfred-Fournier, Paris, on immunity in rabbits infected with the Nichols strain of *Treponema pallidum* the authors concluded that resistance to re-infection is not due to any germicidal activity in the host's tissues, since the strain remained virulent for fresh rabbits for at least 8 to 10 days. In the further experiments now described serial examinations of tissue from inoculated immune rabbits failed to show any inflammatory or phagocytic reaction around the inoculum. It is postulated that there exists a state of "cellular refusal" in which a previously infected organism refuses to accept further amounts of the infecting agent. This type of "cellular memory" is thought to be a fundamental element in immunology. *G. W. Csonka*

Attempts to culture *Treponema pallidum* on Artificial Media. (Züchtungsversuche des *Treponema pallidum* auf künstlichem Nährboden.) MEINICKE, K. (1956). *Hautarzt*, **7,** 407. Bibl.

GONORRHOEA

Gonorrhoea in Men treated with 300,000 Units Procaine Penicillin G. [In English.] GJESSING, H. C. *Acta derm.-venereol. (Stockh.)*, **36,** 122. 1 ref.

A total of 1,115 cases of gonorrhoea in the male were treated between 1949 and 1955 at the Venereal Department of the Bureau of Public Health, Oslo, with various preparations containing procaine benzylpenicillin in a strength of 300,000 units per ml. The patients were given one injection of 300,000 units and advised to abstain from alcohol for a week and to remain under surveillance for at least 30 days. Because many of the patients were sailors or had no fixed address, only 767 completed the follow up. Relapse occurred in 29 and re-infection in twenty cases. The relapse rate for the five preparations of procaine benzylpenicillin used varied from 2·2 to 4·1 per cent. with an over-all relapse rate of 3·8 per cent. in the 767 patients followed up. Many of the patients had had gonorrhoea previously for which they had received penicillin, but their response to treatment in the present investigation differed in no way from that of patients who had not been infected previously. In the cases in which there was a relapse two further injections of 300,000 units were given, with cure in all of them.

[The author admits the difficulty of distinguishing a relapse from a re-infection, and does not describe any local cause for the so-called relapses—for example, littritis.] *Douglas J. Campbell*

An Experiment in the Treatment of Chronic Gonorrhoea in Women with Intracutaneous Injections of a Mixture of Procaine Penicillin, Gonococcal Vaccine, and Methylene Blue. [In Russian.] SHATOV, V. A., GUKHMAN, E. L., OSOVETS, T. O., and GRITSKEVICH, A. N. (1956). *Vestn. Vener. Derm.*, 33. 1 fig, 22 refs.

An experiment was carried out at the Ukraine Institute of Experimental Dermatology and Venereology in the application to the treatment of gonorrhoea in the female of Pavlov's theories concerning the trophic and regulatory functions of the nervous system. It has long been established that irritation of the skin at certain points may lead to trophic changes in corresponding internal organs. Such "active" cutaneous points for the female genitalia are located over the symphysis pubis, the inguinal ligaments, the anterior-superior iliac spines, along the crest of the ilium, and within the limits of Michaelis's rhomboid. At these points the authors inject intracutaneously 0·2 ml. of a mixture of procaine penicillin, methylene blue, and gonococcal vaccine, each dose containing 15,000 units penicillin, 1 mg. methylene blue, and 20×10^6 gonococcal bodies.

The treatment starts with one injection above the pubis, followed the next day by two injections, one on either side of the first, on the third day by three injections, and so on until on the 10th day ten injections are given. Altogether, 55 injections are given at different points, making a total of 825,000 units penicillin, 11×10^8 gonococcal bodies, and 55 mg. methylene blue. The local reaction at the site of injection—erythema and infiltration—has usually disappeared completely by the 10th day.

A general reaction in the form of general malaise with or without a slightly elevated temperature was observed in 62·5 per cent. of the authors' 318 cases, mostly on the 2nd or 3rd day, but occasionally on the 10th day. Exacerbation of the gonorrhoeic process was observed in 37 per cent. of their cases, mostly between the 2nd and 5th days, more rarely between the 6th and 10th days. In the remaining patients improvement started between the 4th and 10th days, but was sometimes delayed up to the 30th day. At the same time local treatment, consisting in daily irrigation of the urethra with silver preparations, and daily swabbings of the cervix uteri with hydrogen peroxide and silver salts, is carried out.

Of the 318 cases treated by this method, in 245 the diagnosis was confirmed bacteriologically. The duration of infection ranged from 3 months to 3 yrs and longer. The follow-up period was up to one year, with a minimum of six bacteriological examinations during that time. Out of 286 patients followed up, 264 (92·3 per cent.) were curcd. *H. Makowska*

Blennorrhoea Neonatorum. [In Dutch.] SMIT, J. A., and VON WERING, R. F. (1955). *Ned. T. Geneesk.*, **99**, 3680.

The incidence of gonorrhoea in Holland has become very low and consequently blennorrhoea neonatorum is practically non-existent. It seems questionable whether it is still advisable to carry out prophylactic treatment of newborn children with silver nitrate.

J. ten Doesschate

Gonorrhoea treated in the Venereological Out-Patient Department during the Years 1950–55. [In English.] NORGAARD, O. (1956). *Acta derm.-venereol. (Stockh.)*, **36**, 150. 16 refs.

Gonorrhoea. Treatment with a Triple Penicillin Combination. WHERRITT, H. R., ALTHEIDE, H. E., and DUFFETT, N. D. (1956). *Missouri Med.*, **53**, 767. 2 refs.

Treatment of Chronic Gonococcal Urethritis in the Male with Chloramphenicol. RANADE, S. N. (1956). *J. Indian med. Ass.*, **27**, 242. 2 refs.

Use of Butazolidin in Gonococcal Arthritis. BURNS, N. P. (1956). *Med. J. Malaya*, **10**, 313. 17 refs.

NON-GONOCOCCAL URETHRITIS AND ALLIED CONDITIONS

Toxic Urethritis. PURCELL, F. W. F. (1956). *S. Afr. J. Lab. clin. Med.*, **2**, 168. 7 refs.

In this paper from Groote Schuur Hospital, Cape Town, the author expresses the view that non-specific urethritis is not a venereal disease, and that to associate the condition with sexual intercourse is both "misleading and retrogressive". Non-gonococcal urethritis, he considers, is almost always non-venereal in origin, the causative organisms and toxins being carried by the blood stream from distant foci of infection—for example, the upper respiratory tract and the bowel, to the prostate, seminal vesicles, and the glands of Cowper, whence infected secretions periodically invade the urethra.

Treatment, which may have to be supplemented by irrigation and urethral dilatations, consists in massaging the glands of Cowper or the prostate, antibiotics being given only when there is evidence of blood-stream infection or when massage is thought to have aggravated the patient's symptoms. The author considers that the demonstration of the presence of a toxin would be a greater advance in the study of the aetiology of non-specific urethritis than the identification of a putative specific organism.

G. L. M. McElligott

Place of Viral Infections among the Non-Gonococcal Forms of Urethritis. (Les urétrites à virus, leur place parmi les autres urétrites non gonococciques.) DUREL, P., and SIBOULET, A. (1956). *Proph. sanit. morale*, **28**, 191. 23 refs.

Reiter's Syndrome. [In French.] BONNET, P., and MOREAU, P.-G. (1955). *Bull. Soc. Ophtal. Paris*, No. 3, 181.

Recurrent Retinitis in Reiter's Disease. MATTSSON, R. (1955). *Acta ophthal. (Kbh.)*, **33**, 403. 16 refs.

CHEMOTHERAPY

Penicillin by Mouth. Laboratory Studies of Absorption of Penicillin V. RINSLER, M. G., and CUNLIFFE, A. C. (1956). *Lancet*, **2**, 328. 2 figs, 20 refs.

Phenoxymethylpenicillin ("penicillin V") has been shown to be relatively stable in an acid milieu. In this paper from King's College Hospital and Medical School, London, the authors report the results of laboratory studies of absorption of this antibiotic after oral administration in various doses, and compare the serum penicillin levels with those obtained after oral administration of similar doses of benzylpenicillin. It was assumed that 1 mg. phenoxymethylpenicillin had an activity approximately equivalent to that of 1,700 units benzylpenicillin.

The blood penicillin levels after administration of 200,000 units phenoxymethylpenicillin were in general equal to those attained after twice this dose of benzylpenicillin. The highest level of the latter was usually reached within an hour, but phenoxymethylpenicillin was absorbed more slowly, the peak concentration being reached only after 1 to 2 hrs. A detectable amount was maintained in the blood for 4 to 6 hrs. One hour after ingestion of 200,000 units phenoxymethylpenicillin the mean serum penicillin level in 29 healthy volunteers was 1·28 unit per ml., while after a similar dose of benzylpenicillin it was only 0·28 unit per ml., and after 400,000 units it was 0·49 unit per ml. When the serum penicillin levels were plotted against the dose per unit body weight there was a more pronounced rise in the level with an increase in dose of phenoxymethylpenicillin than with benzylpenicillin, but even on a dose/weight basis the range of blood penicillin levels for a given amount of phenoxymethylpenicillin was still very considerable. The total daily dose by mouth of phenoxymethylpenicillin should be at least twice the dose of crystalline penicillin given parenterally.

A. Ackroyd

Therapeutic Value in Man of a Combination of Trisulphadiazine and Aureomycin. (L'association trisulfadiazine-auréomycine. Son intérêt actuel en thérapeutique humaine.) PILLOT, J., and TRIBALAT, A. (1956). *Presse méd.*, **64**, 830. 28 refs.

The authors argue that the use of an association of antibacterial agents may have many advantages, mainly in reducing the risk of creating drug resistance in the organism concerned and of intolerance and toxic effects in the patient, and possibly in allowing synergic action and widening of the antimicrobial spectrum. They have therefore studied the antimicrobial effects *in vitro* and *in vivo* of combinations of three sulphadiazines with varying amounts of aureomycin on various types of

micro-organism. The sulphadiazines were selected on account of the infrequency with which they cause toxic effects and the comparative rarity of natural or acquired resistance to them among the common pathogenic organisms.

Laboratory tests having shown some evidence of synergism against cultures and animal infections of various types. The effects of this drug combination were tried in cases of acute and chronic urethritis in males (and also in cases of pulmonary infection and breast abscess). Excellent results are claimed in the treatment of urethritis, both acute and chronic, gonococcal and non-specific [but precise details which would permit comparison with other therapeutic agents are lacking]. The dosage employed was 0·5 to 1 g. aureomycin with 2 to 4 g. triple sulphadiazines daily. Treatment was usually continued for 2 to 3 days and never longer than 6 days.

[The principle of using combinations of antimicrobial agents is generally accepted, and further investigations to determine the optimum proportions of synergistic drugs may well prove profitable, especially in the treatment of chronic genito-urinary infections with a mixture of organisms.] *Robert Lees*

PUBLIC HEALTH AND SOCIAL ASPECTS

Trend in Age of acquiring Venereal Disease in New York City, 1940–1954. ROSENTHAL, T., and VANDOW, J. E. (1956). *N.Y. St. J. Med.*, **56**, 3154. 3 figs, 1 ref.

Prevalence of Venereal Diseases in British West Africa. WILLCOX, R. R. (1956). *W. Afr. med. J.*, **5**, 103. 21 refs.

MISCELLANEOUS

"Unitarian Concept" of the Treponemal Diseases. MOSCHELLA, S. L. (1956). *U.S. armed Forces med. J.*, **7**, 1101. 45 refs.